Remarks

Amendment to the claims

Following the Examiner's suggestion, claim 15 is amended to include the lightpipe element and define its structural and functional relationship to the other elements of the instrument. For clarity purposes, claim 15 is further amended to organize elements in excitation and detection units. Claim 15 also now specifies that the excitation and detection units are located in separate housings. Support for these amendments are found for example in the embodiment depicted on Figure 4 of the patent application as originally filed. It is not the Applicant's intention to limit the scope of claim 15 to the specific embodiment of Figure 4 only. Also, the expression "characterized in that" has been replaced by "wherein" to better accord the US patent practice. No new matter has been added by this amendment, entry is respectfully requested. With entry of the instant amendment claims 15-17 are pending and under consideration.

Claim rejections under 35 U.S.C. §103

Claims 15-17 were rejected under §103(a) as being unpatentable over Bell and Ranford-Cartwright (2002) Trends in Parasitology, v.18(8), pp. 337-342, as evidenced by Wittwer et al. (1997) Biotechniques, v.22(1) pp. 176-181, in view of Hiratsuka et al. (2002) Clin. Biochem., v.35(1), pp. 35-40, Epstein et al. (2002) Anal. Chim. Acta, v.469, pp. 3-36 and Glazer et al., U.S. Patent No. 6,150,107 and Pinkel, U.S. Patent No. 5,837,196.

Before commenting on the prior art, Applicants would like to explain the principle of operation of the invention. The invention aims at a real time PCR instrument for detecting maximum fluorescence emission of at least five different fluorescent compounds. Referring to Figure 4 as an example of possible embodiment for the instrument of the invention, the instrument has an excitation unit comprising a light source (LED) that emits light toward a reaction vessel. A lightpipe is arranged for receiving the light from the reaction vessel and is capable of distributing this light homogeneously to a fiber bundle. The fiber bundle (at least 5) transmits this light to at least 5 separate fluorescent detector entities in the detection unit, each of said detector entities having central detection wavelengths distinct from each other by at least 25 nm. The instrument has also means for heating and cooling and multiple reaction vessels to conduct the necessary heating and cooling steps of the PCR reaction. The excitation and the detection units are located in separate housings.

In response to the Examiner's suggestion to more specifically define the instrument of the structure of the invention, Applicants believe that the elements of the instrument of invention are now defined both structurally and functionally.

There are many advantages provided by the specific arrangement of the instrument according to the invention. One of these advantages is that only one light source, e.g. a monochromatic light source such as for example a LED emitting at 470 nm, is potentially necessary for detecting the fluorescence of at least 5 different fluorescent compounds simultaneously in multicolor real time PCR reactions. The instrument requires neither multiple excitation light sources (with different wavelengths) nor filters for exciting different fluorescent compounds. Because the excitation and detection units are decoupled by using optical fibers and a lightpipe homogeneously distributes the light to these fibers, highly precise positioning of the excitation unit towards the reaction vessel can be achieved without moving the detection unit. Also, the number of necessary dichroic mirrors is minimized by this arrangement.

This is clearly stated on page 17, lines 19-27 of the patent application as filed:

> *"This set up of excitation unit and detection unit located in separate housings provides two advantages compared to the optical unit as disclosed in WO 97/46712: Homogeneous distribution of emitted light into all six detection channels and mechanical decoupling of the excitation and detection unit. This enables highly precise positioning of the excitation unit towards the reaction vessels to become monitored (e. g. capillary tips) without moving the detection unit. Moreover, the number of necessary dichroic mirrors is minimized. An example of such a set up is shown in fig. 4, which discloses a possible embodiment of the invention. As it can be seen, excitation and detection unit are located in different housings."*

Applicants believe that these features are fully reflected in amended claim 15 and that the amendment completely obviates the rejection under 35 U.S.C. 103(a). In particular, none of the prior art of records discloses or teaches this specific arrangement. More specifically, Wittwer et al. disclose two types of instruments, a prototype using one light source an dichroic filters on page 177 and a commercial LightCycler® using multiple light sources. In both embodiments, the excitation unit comprising the light source and the detection unit are located in the same housing. Also, Wittwer et al. does not disclose the use of optical fibers. In fact, Wittwer et al. fails to teach most of the claimed elements of the instrument of the invention.

Bell et al. teach detection of dual hybridization probes using a LightCycler® or an ABI PRISM 7700®. The LightCycler® is precisely the device described by Wittwer and the ABI PRISM 7700® has the same principle of operation as the LightCycler®. In particular, the ABI PRISM 7700® uses multiple light sources and multiple filters for excitation. The ABI PRISM 7700® further fails to teach optical fibers and separate housings for the excitation and detection units. Therefore Bell et al. do not cure the defects of Wittwer as explained above.

Pinkel et al. teach a bundle of optical fibers dipped in the reaction medium and transmitting directly the light emitted from the reaction vessel to multiple detectors. Apart from teaching the use of optical fibers in a detection method, Pinkel et al. does not provide any teaching that could be useful to arrive at the invention. In particular, the device taught in Pinkel et al. is completely inadequate for the intended purpose of the instrument according to the invention, which is detecting the fluorescence of at least 5 different fluorescent compounds simultaneously in multicolor real time PCR reactions. There is no element allowing a real time PCR reaction in the device taught by Pinkel et al. Further, Pinkel et al. does not teach the benefits of the instrument according to the invention regarding the separation of the excitation and detection units, the precision obtained and the minimization of dichroic mirrors. Therefore, the person skilled in the art would not even have been motivated to take into account the teaching of Pinkel et al.

Epstein et al. and Glazer et al. do not provide any additional teaching in this regard either.

Applicants therefore respectfully submit that the instrument as presently claimed in claim 15 is not obvious over the prior art of records. Reconsideration and withdrawal of the obviousness rejection of claim 15 under §103(a) as being unpatentable over Bell and Ranford-Cartwright (2002) Trends in Parasitology, v.18(8), pp. 337-342, as evidenced by Wittwer et al. (1997) Biotechniques, v.22(1) pp. 176-181, in view of Hiratsuka et al. (2002) Clin. Biochem., v.35(1), pp. 35-40, Epstein et al. (2002) Anal. Chim. Acta, v.469, pp. 3-36 and Glazer et al., U.S. Patent No. 6,150,107 and Pinkel, U.S. Patent No. 5,837,196 are respectfully requested.

Claims 16 and 17 depend upon claim 15 and therefore incorporate each and every limitation of that claim. For the reasons set forth with respect to claim 15, withdrawal of the rejections of the dependent claims 16 and 17 is also respectfully requested.

Conclusion

In view of the above, Applicants believe that all claims now pending in this application are in condition for allowance. The shortened statutory period of three months originally set for responding to the Non Final Office mailed November 12, 2008 expired on February 12, 2009. Applicants respectfully request a 1-month. The extension of time resets the deadline for responding to March 12, 2009. The Commissioner is hereby authorized to charge the fee due under 37 CFR § 1.17(a)(1), to Deposit account No. 50-0812.

It is believed that no other fees are due at this time. However, the Commissioner is authorized to charge any fee deficiency or credit any overpayment to Deposit Account No. 50-0812.

If the Examiner believes that a telephone conference would expedite prosecution of this application, please call the undersigned at the number below.

Respectfully submitted,

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